Initial Approval: July 8, 2020
Revised Dates: April 21, 2021;
October 14, 2020

CRITERIA FOR PRIOR AUTHORIZATION

Duchenne Muscular Dystrophy (DMD) Agents

BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES Prior authorization will be required for all current and future dose forms available. All medication-specific criteria, including drug-specific indication, age, and dose for each agent is defined in Table 1 below.

Casimersen (Amondys 45™)
Deflazacort (Emflaza®)
Eteplirsen (Exondys 51™)
Golodirsen (Vyondys 53™)
Viltolarsen (Viltepso®™)

GENERAL CRITERIA FOR INITIAL PRIOR AUTHORIZATION (must meet all of the following):

- Must be approved for the indication, age, and not exceed dosing limits listed in Table 1.
- Medication is prescribed by or in consultation with a prescriber specializing in the treatment of DMD (i.e., neurologist, pediatric neurologist, or physical medicine and rehabilitation specialist).[3]
- For all agents listed, the preferred PDL drug, which treats the PA indication, is required unless the patient meets the non-preferred PDL PA criteria.
- Prescriber must provide the patient's current baseline weight (required for dosing).
- For glucocorticoids, must meet ALL of the following:
  - Patient must have a trial of prednisone at the dose of 0.75 mg/kg/day or 10 mg/kg/weekend for at least 3 months.[3,11]
  - Prescriber must provide compelling rationale of why the patient will benefit from deflazacort over prednisone. Note: less weight gain is not an accepted rationale.
- For antisense oligonucleotides:
  - Prescriber must provide genetic testing results confirming the mutation of the DMD gene is amenable to exon 45, exon 51 or exon 53 skipping.[6,7,15~~5,6~~]
  - Patient is not taking with any other RNA antisense oligonucleotide agent or any other gene therapy.
  - Patient must maintain their current corticosteroid status. Must meet ONE of the following:
    - Patients must be established on corticosteroid therapy (for at least 6 months) and continue on the same corticosteroid regimen throughout the initial approval period until renewal is approved or until the antisense oligonucleotide is discontinued, whichever comes first.
    - Patients who choose not to be treated with corticosteroids must agree to not start any corticosteroids until renewal is approved or until the antisense oligonucleotide is discontinued, whichever comes first.
  - Prescriber must provide one of the following baseline function test results that is age-appropriate for the patient:[3]
    - North Star Ambulatory Assessment (NSAA) (3 years of age and older).
    - 6-minute walk test (6MWT) (ages 2 years of age and older, ambulatory).
    - Brooke Upper Extremity Scale (ages 1-5 years, onset of muscle weakness prior to age 5).
    - Egen Klassifikation Scale (ages 2-70 years, non-ambulatory).
    - Reachable workspace (ages 7-23 years, non-ambulatory).
    - Performance of Upper Limb Test (ages 5 years and older, both ambulatory and non-ambulatory).

- Bayley Scales of Infant Motor Development III or IV (Infants aged 1 to 42 months).

CRITERIA FOR RENEWAL PRIOR AUTHORIZATION: (must meet all of the following)

- Must not exceed dosing limits listed in Table 1.
- Prescriber has provided the patient's current weight (required for dosing).
- For glucocorticoids:
  - Prescriber attests that the patient is benefitting from therapy.
- For antisense oligonucleotides:
  - Patient is not taking with any other RNA antisense oligonucleotide agent or any other gene therapy. Must meet one of the following:
    - Prescriber must provide the same function test that was submitted with the initial approval, demonstrating the patient has experienced clinical improvement or remained stable compared to baseline.[3]
    - Improvement is defined as one or more of the following:
      - Increase score in the following: North Star Ambulatory Assessment (NSAA), 6-minute walk test (6MWT), Reachable workspace, Performance of Upper Limb Test, Bayley Scales of Infant Motor Development III or IV
      - Decrease score in the following: Brooke Upper Extremity Scale, Egen Klassifikation Scale

LENGTH OF APPROVAL (INITIAL AND RENEWAL): 12 months

FOR DRUGS THAT HAVE A CURRENT PA REQUIREMENT, BUT NOT FOR THE NEWLY APPROVED INDICATIONS, FOR OTHER FDA-APPROVED INDICATIONS, AND FOR CHANGES TO AGE REQUIREMENTS NOT LISTED WITHIN THE PA CRITERIA:

- **THE PA REQUEST WILL BE REVIEWED BASED UPON THE FOLLOWING PACKAGE INSERT INFORMATION: INDICATION, AGE, DOSE, AND ANY PRE-REQUISITE TREATMENT REQUIREMENTS FOR THAT INDICATION.**

LENGTH OF APPROVAL (INITIAL AND RENEWAL): 12 months

Table 1. FDA-approved age and dosing limits of DMD Agents.[5-7,12,15]

Medication	Indication(s)	Age	Dosing Limits
Antisense Oligonucleotides			
Casimersen (Amondys 45™)	DMD with a confirmed mutation of the DMD gene that is amenable to exon 45 skipping	N/A	30 mg/kg IV once weekly.
Eteplirsen (Exondys 51™)	DMD with a confirmed mutation of the DMD gene that is amenable to exon 51 skipping	N/A	30 mg/kg IV once weekly.
Golodirsen (Vyondys 53™)	DMD with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping	N/A	30 mg/kg IV once weekly.
Viltolarsen (Viltepso®™)	DMD with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping	N/A	80 mg/kg IV once weekly.
Glucocorticoids			
Deflazacort (Emflaza®)	DMD	≥ 2 years	0.9 mg/kg orally once daily.

IV: intravenous

Notes:

Amondys 45™	This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Amondys 45™. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.[17] The ESSENCE trial (NCT02500381) is suspected to be the new trial to confirm clinical benefit and is expected to be completed 4/2024 with a final report submission 10/2024.[16]
Exondys 51™	A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.[5] ~~In order to verify the clinical benefit of eteplirsen, a 2-year trial must be completed, which is expected 11/2020 with a final report submission 5/2021.[8]~~ A new confirmatory trial (MISS51ON , NCT03992430) is active and is expected to be completed in 2026.[18]
Vyondys 53™	This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.[7] ~~In order to verify the clinical benefit of golodirsen, Study 4045-301 must be completed, which is expected 4/2024 with a final report submission 10/2024.[9]~~ The ESSENCE trial (NCT02500381) is suspected to be the new trial to confirm clinical benefit and is expected to be completed 4/2024 with a final report submission 10/2024.[16]
Viltepso®™	This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Viltepso. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.[14] In order to verify the clinical benefit of viltolarsen, ~~Study NS-065/NCNP-01~~ the RACER53 trial (NCT04060199) must be completed, which is expected 12/2024.[13]
Corticosteroids	Prednisone and deflazacort may be equivalent in improving strength and timed motor function, improving pulmonary function, reducing the need for scoliosis surgery, and delaying the onset of cardiomyopathy by 18 years of age.[1] Deflazacort and prednisone show slightly different adverse event profiles in studies where each drug was compared with no treatment or the drugs were compared with each other:[1] • Weight gain in the first years of treatment and cushingoid appearance may occur more frequently with prednisone. • Cataracts are more frequently reported with deflazacort. Other adverse events were not significantly different between the 2 groups, including behavioral changes, gastric symptoms, hypertension, glucose control, and hirsutism.[1] Because most DMD patients are expected to be on corticosteroids long-term, any benefit from deflazacort's delayed weight gain effect appears to be lost after approximately 1 year.[1]

	It is unclear if there are detrimental effects of weight gain due to corticosteroid use in DMD patients, per the 2005 Practice Parameter.[2] A 1993 RCT was cited where prednisone-treated patients were found to have a 36% increase in muscle mass compared to placebo at 18 months. The 2018 guidelines from Lancet Neurology list "failure to thrive or poor weight gain" as a common early sign/symptom when suspecting that a patient has DMD.[3] A recently completed phase 3 study may provide more clarity on how to manage corticosteroid use in DMD patients. See the Finding the Optimum Regimen for Duchenne Muscular Dystrophy (FOR-DMD) ClinicalTrials.gov Identifier: NCT01603407.[10]

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DRUG UTILIZATION REVIEW COMMITTEE CHAIR	PHARMACY PROGRAM MANAGER DIVISION OF HEALTH CARE FINANCE KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT
DATE	DATE